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Dr Joshua Lederberg
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Dear Josh:

We have recently finished a study of the distribution of plasmids related to F in natural isolates of *E. coli* that has caused me to speculate on the origin of the F factor in laboratory strains. The thought is summarized in the following passage from the Discussion of the paper I am working on. I am hoping that you will have a look at it and tell me whether you think the scenario is plausible and, if not, why not.

"Our data also bear on the history of the F factor in laboratory strains. It has often been remarked that LEDERBERG was extremely lucky to use a strain in which the F factor was derepressed owing to an insertion of IS*3* in the *finO* gene. However, the frequency of F-related plasmids in the ECOR strains shows that there is a reasonable chance that any randomly selected strain might have such a plasmid: 7 percent of the ECOR strains have an F plasmid and 11 percent have an R plasmid. What is remarkable in the laboratory F factor is the insertion mutation in *finO*. In our PCR amplifications of the 28 *finO* genes in plasmids in the ECOR collection, not one produced a product other than the expected size. When did the insertion in the laboratory F factor take place? Probably not in nature. We suspect that it happened in LEDERBERG'S own laboratory as various subcultures of K-12 were isolated and examined for their ability to undergo recombination. Any subculture with an insertion in *finO* would be a good at recombination, and such a strain would certainly have been used in further experiments. Hence, a chance insertion of IS*3* interrupting *finO* may well have been the result of unconscious selection -- a case of chance favoring the prepared mind."

Many thanks for your consideration.

Best regards,

Daniel L. Hartl
Professor of Biology